Department of Pharmacology
Application
Thomas Collum Butler Fellowship
(Deadline: FRIDAY, November 21, 2008)

Name: Eric Zimmerman

Mentor: Lee Graves, Ph.D.

Graduate Program/Entering Date: Pharmacology, Fall 2006

Brief State of Research Interests (1 page maximum):

The balance between cell viability and programmed cell death is fundamental to maintaining cellular homeostasis. Many disease states such as cancer, neurodegenerative disorders, and developmental disorders, at their basic elements, can be characterized by a disruption of cellular homeostasis. Therefore, it is imperative that researchers understand how cells control their fate in order to better combat disease.

The focus of my dissertation research is to elucidate the role of tyrosine kinase signaling in mitochondria-mediated cell death (intrinsic apoptosis). Using a cancer cell line that is resistant to drug-induced apoptosis, I am 1) profiling the tyrosine "phospho-proteome" using quantitative proteomics and 2) measuring the expression of microRNAs and comparing this to microRNA levels in drug-sensitive cells. I hypothesize that tyrosine kinase signaling events can directly or indirectly modify mitochondrial machinery involved in apoptosis in order to prevent cell death. MicroRNAs may mediate these events as effectors of tyrosine kinase signaling or, alternatively, may impinge upon tyrosine kinase expression to alter signaling properties. Nevertheless, the connection between kinase signaling and microRNA networks is a novel and innovative method to understand molecular adaptation of apoptotic machinery.

State How Your Work Relates to Developmental Disabilities (1 paragraph):

Programmed cell death is a basic and fundamental mechanism intrinsic to the cell. Cell death due to the disruption of apoptotic machinery provides the pathological basis for many developmental disabilities including mental retardation and ataxia. Therefore, understanding the molecular mechanisms by which cells can escape or induce apoptosis will provide therapeutic targets for the prevention and treatment of developmental disorders.

List Publications, Abstracts, Awards:

Publications:

Zimmerman EI, Huang M, Leisewitz AV, Wang Y, Yang J, and Graves LM. Identification of a novel point mutation in ENT1 that confers resistance to Ara-C in human T cell leukemia CCRF-CEM cells. *FEBS Lett.* 2009 Jan;583(2):425-9.

Leisewitz AV, **Zimmerman EI**, Jones SZ, Yang J, and Graves LM. Imatinib-resistant CML cells have low ENT activity but maintain sensitivity to gemcitabine. *Nucleosides Nucleotides Nucleic Acids*. 2008 Jun;27(6):779-86.

Fischer BD, **Zimmerman EI**, Picker MJ, and Dykstra LA. Morphine in combination with metabotropic glutamate receptor antagonists on schedule-controlled responding and thermal nociception. *J Pharmacol Exp Ther.* 2008 Feb;324(2):732-9

Abstracts:

Zimmerman EI, Leisewitz A, Huang M, and Graves LM. (April 2008) Amino acid residue 24 of the human equilibrative nucleoside transporter 1 (ENT1) is important for transport activity. *2008 Experimental Biology Meeting,* San Diego, CA

Zimmerman EI, Zitzman D, Fish EW, Faccidomo S, Yap JJ, Tornatzky W, and Miczek KA. (September 2006) Effects of $GABA_A$ receptor agonists and NMDA receptor antagonists on maternally-isolated mouse pup ultrasonic vocalization. *2006 Society for Neuroscience Conference,* Atlanta, GA

Zimmerman EI, Zitzman D, and Miczek, KA. (April 2005) Effects of GABA-ergic compounds on ultrasonic vocalizations in mouse pups: modulation at the $GABA_A$ α_2 subunit. *2005 Northeast Undergraduate Research Organization for Neuroscience Conference,* Hunter College, New York, NY

Awards:

2008 – Cell and Molecular Biology (CMB) Collaboration Grant